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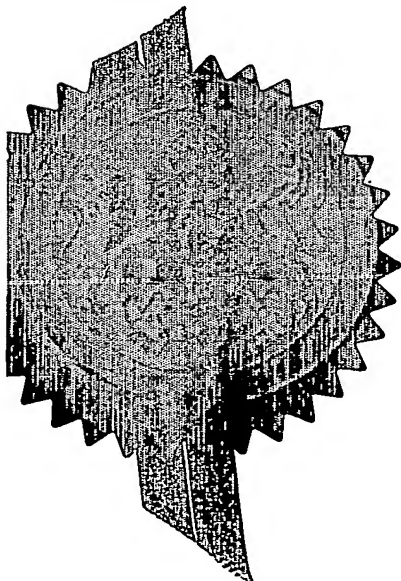
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Signed

L. Mahoney

Dated 25 June 2003

06 AUG 2002

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The Patent Office

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06 AUG 2002

1.	Your reference	4-32607P1		
2.	Patent application number (The Patent Office will fill in)	0218244.2		07AUG02 E739018-3 D00524 P01/7700 0.00-0218244.2
3.	Full name, address and postcode of the or of each applicant (underline all surnames)	NOVARTIS AG LICHTSTRASSE 35 4056 BASEL SWITZERLAND		
	Patent ADP number (if you know it)			
	If the applicant is a corporate body, give the country/state of its incorporation	SWITZERLAND		
4.	Title of invention	Organic compounds		
5.	Name of your agent (If you have one)			
	"Address for service" in the United Kingdom to which all correspondence should be sent (including the postcode)	B.A. YORKE & CO. CHARTERED PATENT AGENTS COOMB HOUSE, 7 ST. JOHN'S ROAD ISLEWORTH MIDDLESEX TW7 6NH		
	Patents ADP number (if you know it)	1800001		
6.	If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and (if you know it) the or each application number	Country	Priority application number (if you know it)	Date of filing (day/month/year)
7.	If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application	Number of earlier application	Date of filing (day/month/year)	
8.	Is a statement of inventorship and of right to grant of a patent required in support of this request? (Answer 'Yes' if:	Yes		
	a) any applicant named in part 3 is not an inventor, or			
	b) there is an inventor who is not named as an applicant, or			
	c) any named applicant is a corporate body.			
	(see note (d))			

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Patents Form 1/77

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Continuation sheets of this form

Description 3

Claim(s) 1

Abstract 1

Drawing(s)

10. If you are also filing any of the following, state how many against each item.

Priority documents

Translations of priority documents

Statement of inventorship and right to grant of a patent (*Patents Form 7/77*)

Request for preliminary examination and search (*Patents Form 9/77*) ONE

Request for substantive examination (*Patents Form 10/77*)

Any other documents
(please specify)

11.

I/We request the grant of a patent on the basis of this application

Signature

Date

B. A. Yorke & Co.

B.A. Yorke & Co.

06 August 2002

12. Name and daytime telephone number of person to contact in the United Kingdom

Mrs. E. Cheetham
020 8560 5847

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Organic Compounds

The present invention relates to new pharmaceutical uses of a carbamazepine derivative.

More particularly the present invention relates to new pharmaceutical uses for the carbamazepine derivative of formula I



and their pharmaceutically acceptable salts, hereafter referred to as "the compound".

MHD (10-hydroxy-10,11-dihydro-carbamazepine), the main metabolite of the antiepileptic oxcarbazepine (Trileptal[®]) is well known from the literature [see for example Schuetz H. et al., Xenobiotica (GB), 16(8), 769-778 (1986)] and can be prepared synthetically starting from oxcarbazepine according to conventional methods. Monohydroxycarbamazepine has been first disclosed in GB 1310120. The compound is indicated to be suitable for the treatment of psychosomatic disturbances, epilepsy, trigeminal neuralgia and cerebral spasticity.

In accordance with the present invention, it has now surprisingly been found that the compound of formula I in free base or acid addition salt is also useful in the prevention and treatment of tinnitus and other inner ear/cochlear excitability related diseases such as neuronal loss, hearing loss, sudden deafness, vertigo or Meniere's disease.

The activity in tinnitus of the compound is indicated in standard tests, e.g. in the salicylate-induced tinnitus model.

It has been demonstrated [C.A. Bauer et al., Hearing Research 147 (2000) 175-182] that chronic salicylate exposure causes upregulation of glutamic acid decarboxylase (GAD) expression in the rat inferior colliculus (IC), associated with the development of tinnitus. Furthermore, electrophysiological recordings from auditory neurons using patch clamp recording techniques [D. Peruzzi et al. Neuroscience 101 (2000) 403-416, X. Lin et al.,

Journal of Neurophysiology 79 (1998) 2503-2512] and single neuron recordings [J.J. Eggermont and M. Kenmochi, Hearing Research 117 (1998) 149-160] showed that the excitability of neurons is changed following salicylate and quinine treatment.

Administration of salicylate or quinine caused an increase in the firing rate auditory neurons measured by extracellular electrophysiological recording techniques. Using in vitro electrophysiological recording techniques superfusion with salicylate increases the excitability of the recorded neurons. On administration of the compounds at concentrations of about 1nM to 300 μ M, the effects of salicylate were reversed.

For the treatment of tinnitus, appropriate dosage will of course vary depending upon, for example, the compound employed, the host, the mode of administration and the nature and severity of the condition being treated. However, in general, satisfactory results in animals are indicated to be obtained at a daily dosage of from about 1 to about 300 mg/kg animal body weight. In larger mammals, for example humans, an indicated daily dosage is in the range from about 10 to about 3000 mg of a compound according to the invention, conveniently administered, for example, in divided doses up to four times a day.

The compounds may be administered in any usual manner, e.g. orally, for example in the form of tablets or capsules, or parenterally, for example in the form of injection solutions or suspensions.

The present invention also provides pharmaceutical compositions comprising the compounds in association with at least one pharmaceutical carrier or diluent for use in the treatment of tinnitus. Such compositions may be manufactured in conventional manner.

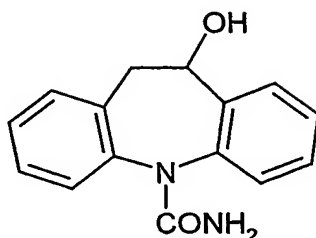
Unit dosage forms may contain for example from about 2.5 mg to about 1000 mg of the compound.

The invention further provides the use of a compound according to the invention for the manufacture of a pharmaceutical composition for the treatment of tinnitus and other inner ear/cochlear excitability related diseases such as neuronal loss, hearing loss, sudden deafness, vertigo or Meniere's disease.

The invention further provides a method for the treatment of tinnitus and other inner ear/cochlear excitability related diseases such as neuronal loss, hearing loss, sudden deafness, vertigo or Meniere's disease in a subject in need of such treatment, which comprises administering to said subject a therapeutically effective amount of a compound according to the invention.

CLAIMS

1. The use of a compound of formula I



I

- and their pharmaceutically acceptable salts, for the treatment of tinnitus.
2. A pharmaceutical composition which incorporates as active agent a compound of formula I according to claim 1 in free or pharmaceutically acceptable salt form, for use in the treatment of tinnitus and other inner ear/cochlear excitability related diseases such as neuronal loss, hearing loss, sudden deafness, vertigo or Meniere's disease.
 3. The use of a compound of formula I according to claim 1, in free or pharmaceutically acceptable salt form, for the manufacture of a pharmaceutical composition for the treatment of tinnitus and other inner ear/cochlear excitability related diseases such as neuronal loss, hearing loss, sudden deafness, vertigo or Meniere's disease.
 4. A method for the treatment of tinnitus and other inner ear/cochlear excitability related diseases such as neuronal loss, hearing loss, sudden deafness, vertigo or Meniere's disease in a subject in need of such treatment, which comprises administering to said subject a therapeutically effective amount of a compound of formula I according to claim 1 in free or pharmaceutically acceptable salt form.

Abstract:

The present invention relates to the use of a carbamazepine derivative in treating tinnitus.